REMARKS

The final Office action dated January 15, 2004 is acknowledged. Claims 1-28 are pending in the instant application. According to the Office action, each of claims 1-28 have been rejected. Claims 1, 14 and 15 have been amended to more clearly define the present invention. No new subject matter has been added to these claims. These amendments are minor and clerical in nature, basically saying that the self-adhesive polymer matrix layer is covered (rather than "can be covered") with an active substance-permeable backing layer at the side facing away from the skin. The meaning of these claims is unchanged. The applicant submits that said amendments are supported by Examples 1-3 in the specification, according to which the dried adhesive film (that which contains the active substance) is laminated with a polyester film which serves as a backing layer in the transdermal systems which were punched out from this laminate. Reconsideration is respectfully requested in light of the following remarks and the aforementioned amendments.

Rejection of Claims 1-15 under 35 U.S.C. 103 (a)

Claims 1-28 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,503,844 (Kwiatek et al.). It is respectfully submitted that these claims are patentably distinct from the prior art reference.

The Examiner states that Kwiatek et al. '844 teaches the use of a transdermal therapeutic patch for the controlled release of lovastatin to the skin or mucous membranes, wherein the transdermal patch contains active substance(s), a backing layer, active agent permeable adhesive layer(s), rate-controlling polymers and a means whereby

the transdermal patch has a high degree of uniformity and consistency for critical transdermal properties such as release rate, and refers to col. 1, line 45 – col. 2, line 25; col. 11, line 47 – col. 12, line 55; col. 16, lines 30 – 40; col. 17, lines 5 – 12; and col. 24, lines 20 – 26. The Examiner further states that Kwiatek et al. '844 teaches that each active agent permeable adhesive layer is a pressure-sensitive adhesive layer and that any of the well-known, dermatologically acceptable, pressure-sensitive adhesives that permit drug migration therethrough can be used.

The Examiner also states that Kwiatek et al. '844 teaches that each active agent permeable adhesive layer is a pressure-sensitive adhesive and that any of the well-known, dermatologically acceptable, pressure-sensitive adhesive that permit drug migration therethrough can be used. According to the Examiner, suitable permeable adhesives include acrylic or methacrylic resins, polyisobutylene pressure-sensitive adhesives, rubber pressure-sensitive adhesives, silicon pressure-sensitive adhesives and the like, and tackifiers, stabilizers, active agent flux enhancers, carriers, binders, etc. may also be used in the patch. For these, and the additional reasons set forth on pages 3-5 of the Office action, the Examiner considers the present invention obvious and unpatentable in light of Kwiatek et al. '844.

Applicant respectfully points out that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references when combined must teach or suggest all of the claim limitations.

Regarding Kwiatek et al. '844, the applicant submits that it is taught therein that the non-adhesive cellular foam layer is an essential component of the transdermal patch described in the reference, and that this non-adhesive foam layer contains the bulk proportion of active substance (col. 1, line 61 – col. 2, line 8). In addition, the non-adhesive foam layer is provided with an adhesive layer which serves as a means for affixing the non-adhesive foam layer to the skin. Optionally, this adhesive layer may contain a minor amount of active substance (col. 12, lines 38-48). Lastly, according to Kwiatek et al. '844, the invention was based on the discovery that absorbent cellular foams would be suitable for use as liquid active agent carriers in transdermal delivery patches (col. 3, last paragraph and col. 16, lines 42-50). It is submitted that in all the examples throughout this reference, nicotine (a liquid active substance) was used.

Applicant respectfully disagrees with the Examiner's conclusions set forth above, namely that the present invention is obvious in light of Kwiatek et al. 844. The applicant respectfully submits that claims 1 and 15 (each as amended) pertain to a transdermal therapeutic system in the form of an adhesive patch in which the active substance is incorporated into the adhesive layer, and the side of the adhesive layer which faces away from the skin is covered with an active substance-impermeable backing layer. The applicant submits that from this, it clearly and directly follows that the adhesive layer is the one and only reservoir (for active substances) in the claimed transdermal systems. In particular, the wording of claims 1 and 15 excludes the possibility of an additional foam-type reservoir, as described throughout Kwiatek et al. '844. In the transdermal systems disclosed by Kwiatek et al. '844, a minor portion of the active substance may be

contained in a skin-contacting adhesive matrix layer. However, the side of the adhesive layer which faces away from the skin is not covered with an active substance-impermeable backing layer, but with a cellular foam layer which contains most of the active substance and which is permeable to the active substance.

The applicant also submits that claims 1 and 15, as amended, provide that essentially all of the active substance which is to be released from the transdermal system to the skin is present within the adhesive matrix layer. In contrast, in the transdermal patches described by Kwiatek et al., only a small portion of the total amount of active substance is present in the active substance-permeable matrix layer. The bulk of the active substance in Kwiatek et al. '844 is contained in the foam matrix layer (col. 12, lines 38-48).

Regarding claim 14, the applicant submits that it is a method of treatment using a transdermal therapeutic system as described in claims 1 or 15. Therefore, the above arguments which differentiate the invention as set forth in claims 1 and 15 also apply to claim 14.

Regarding claim 16, the last paragraph therein recites that the backing layer forms the outermost layer of the opposite side of the matrix layer. It is respectfully submitted that claim 16 clearly excludes the possibility that an additional foam matrix layer, as taught in Kwiatek et al. '844, may be included.

As discussed above, Kwiatek et al. '844 teaches that the presence of a cellular foam layer constitutes an essential feature of the invention described therein, and that the foam layer should contain the bulk of the active substance. In contrast, the claims of the

present application recite that all of the active substance is incorporated in an adhesive layer which is covered on its outside by a backing layer, not by a foam layer. As such, the applicant respectfully disagrees with the Examiner's conclusion that there is no significant distinction observed between the instant invention and system described in the prior art in that a feature which is considered to be essential to the prior art invention (the foam layer) is not present at all in the present invention.

The applicant submits that one skilled in the relevant art having referred to Kwiatek et al. '844 for developing a transdermal patch for the delivery of an active ingredient which influences the blood lipid level would have learned from the reference that it would be advantageous to incorporate the active ingredient in liquid form into a non-adhesive foam matrix. In case of a solid active ingredient, one skilled in the art would have understood to dissolve the solid active ingredient in a suitable liquid carrier, and would have impregnated the foam matrix with the obtained solution (Kwiatek et al. '844, col. 16, lines 46-50). However, the applicant submits that nothing within the teaching of Kwiatek et al. '844 suggests that the foam layer could be omitted or that an active agent permeable adhesive layer could be used as the sole active substance reservoir. Moreover, it appears there would be significant doubts that one skilled in the art would have taken the Kwiatek et al. '844 teaching into consideration at all. As noted above, the invention of Kwiatek et al. '844 was made to provide a better method for making transdermal patches which contain liquid active substances, such as nicotine. The applicant submits that one skilled in the art would have considered the use of a foam matrix to have certain advantages in cases where the active substance is normally in its

liquid form. In light of the above arguments, it is respectfully submitted that there would be no motivation for one skilled in the art to have modified the teaching of Kwiatek et al. in order to arrive at the present invention.

The applicant would now like to respond to the additional statements made by the Examiner in the Office action in response to the applicant's previously submitted arguments. It was stated in the Office action that "according to Kwiatek, the rate of permeation of active agent through the rate-controlling polymer layer depends upon factors such as ... affinity of the active agent for the polymer layer ... polymeric structure of the foam layer ..." and "Therefore, the appropriate rate-controlling polymeric material ... depends on the active agent used and the desired rate of permeation."

It is submitted that in the transdermal systems of the present invention, the rate of permeation is mainly determined by the polymer composition of the adhesive reservoir (and optionally may be skin-permeation-enhancing auxiliary substances which optionally may be present in the adhesive reservoir). The structure and function of the adhesive reservoir of the transdermal systems of the present invention are not comparable to the structure and function of the rate-controlling polymer layer described by Kwiatek et al. '844. The Kwiatek et al. '844 rate-controlling layer does not function as a reservoir for active substances (i.e. in Example 2, col. 23 ("polyurethane film layer)). In addition, the transdermal systems of the present invention, the adhesive reservoir acts as a reservoir which at the same time has a permeation rate-controlling function. Therefore, the applicant submits that it is not appropriate to apply the teaching which concerns the rate-

controlling layer to the composition of adhesive polymer reservoir layers as used in the present invention.

Regarding the foam matrix layer described by Kwiatek et al., the applicant respectfully disagrees with the statement that the "polymeric structure of the foam layer" influences the permeation rate of the active substance. The pores appears to be macroscopic (col. 15, lines 48-55); therefore, the polymeric structure will hardly have any influence at all on the release rate. The release rate is controlled by the rate-controlling layer (if present), whereas the active substance-permeable layer is not described as having a rate-controlling function.

The Examiner also stated in the Office action on page 4 that "Kwiatek teaches that the transdermal patch is produced efficiently with little variation in release rate." However, the applicant wishes to point out that according to Kwiatek et al. '844, these properties result from the presence of a cellular foam layer having the active substance incorporated therein, and optionally a rate-controlling layer (col. 1, lines 53-67; col 2, lines 8-17). In contrast, the transdermal therapeutic systems do not comprise a cellular foam layer, and the active substance is contained in an adhesive polymer layer rather than in a cellular foam. Therefore, in view of the teaching of Kwiatek et al. '844, the observation that the release of active substance is essentially constant over a period of at least 72 hours (such as in present claims 1, 14, 15 and 16) when using an adhesive reservoir instead of a foam reservoir is unexpected. Moreover, the conclusion that such a result would be obvious in the system of Kwiatek et al. '844 would be applying

impermissible hindsight reasoning, which is an improper basis for an obviousness-type rejection, as set forth in M.P.E.P. Sec. 2145(X)(A).

On page 6, line 16 of the Office action, the Examiner states that "the foam layer of Kwiatek is a matrix in itself." The applicant respectfully disagrees to the extent that a foam matrix is fundamentally different from an adhesive polymer matrix. A foam matrix is characterized by a plurality of pre-formed inner voids or interstices (Kwiatek et al. '844, col. 13, lines 18-21; col. 15, lines 48-56) which serve as containers for the liquid active substance. An adhesive polymer matrix does not have such voids or interstices. The active substance is homogeneously dispersed or embedded within the polymer molecules which form the adhesive matrix. The voids in the foam reservoir described by Kwiatek et al. '844 are filled with liquid active substance, therefore, the applicant respectfully disagrees with the conclusion that the active ingredient is embedded in the foam (Office action, page 6, last 2 lines). In light of the aforementioned differences between the system of Kwiatek et al. '844 and the system of the present invention, the applicant respectfully disagrees with the Examiner's conclusion that there is no distinction between the foam of Kwiatek et al. '844 and the applicant's matrix layer.

It was lastly pointed out in the Office action (page 7, lines 5-8) that the active agent permeable layer of Kwiatek et al. '844 contains some of the active agent. However, as discussed above, nowhere in the reference is it taught or suggested that this active agent permeable layer could be used as the sold active substance reservoir.

In summary, the applicant does not believe that Kwiatek et al. '844 teaches or suggests the matrix type reservoir system for transdermal administration of active agents

wherein the active agent is dispersed in a self-adhesive polymer matrix which serves as a reservoir for the active-agent as well as a means for adhering the patch to the patient's skin, nor would the same have been obvious to one skilled in the art at the time the present invention was made. It is also apparent that the reference provides no suggestion or motivation to modify the invention of Kwiatek et al. '844 to make up for the aforementioned deficiencies, nor would there be a reasonable expectation of success if one skilled in the art were to attempt to modify the reference.

Conclusion

For the foregoing reasons, it is respectfully submitted the present application is in condition for allowance, and such action is earnestly solicited. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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